Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 16 claims. Claims 7-16 were cancelled as the result of a restriction requirement. Claims 1-6 have been cancelled herein and replaced with new claims 17-36.

II. The Amendments

For the most part, the new claims introduced herein are fully supported by the claims originally filed in the application and which have now been cancelled. Support for claim language referring to integration mutagenesis of the poxB gene may be found in Example 10 of the specification. Support for claims reciting the use of the pCR2.1poxBint plasmid may be found in Examples 10 and 11.

None of the amendments made herein add new matter to the application, and their entry is therefore respectfully requested.

The Rejections

I. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

On page 2 of the Office Action, claims 1 and 6 are rejected based upon the allegation that the term "switched off" is indefinite. The Examiner suggests that the term may be synonymous with "eliminated."

In response, Applicants have amended claims to remove the language objected to by the Examiner. In certain instances, this term has been replaced with the word "eliminated." In light of these amendments, it is submitted that the Examiner's rejection has been overcome, and it is respectfully requested that it be withdrawn.

II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

A. Rejections Based on the Written Description Requirement

On pages 2-4 of the Office Action, all pending claims are rejected under the written description requirement of 35 U.S.C. § 112, first paragraph. The Examiner argues that the specification fails to adequately disclose the structure and function of all zwf genes and all endogenous poxB genes that fall within the scope of the claims. The Examiner also argues that the genus of coryneform bacteria is very large and, apparently as a result, is also not fully described by Applicants.

In response, Applicants have amended claims in a manner which they believe should overcome all of the Examiner's allegations. Claims now define zwf genes and poxB genes by the specific sequences that they encode. In particular, the zwf gene is defined according to SEQ ID NOS:8 and 10. Similarly, the poxB gene is defined according to SEQ ID NO:5. In addition, claims are now limited to the species *Corynebacterium glutamicum*.

In light of the amendments described above, Applicants respectfully submit that the Examiner's rejections with respect to the written description requirement of patentability have been overcome. It is therefore respectfully requested that these rejections be withdrawn.

B. Rejections Based on the Enablement Requirement

On pages 4-8 of the Office Action, all pending claims are rejected based upon the enablement requirement of 35 U.S.C. § 112, first paragraph. The Examiner argues:

> Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making lysine using *Corynebacterium glutamicum* containing an inactivating deletion in the endogenous poxB gene and transformed with a nucleic acid encoding the zwf protein of SEQ ID NO:10, does not reasonably provide enablement for methods of making any amino acid using any coryneform bacteria in which the activity of the pyruvate oxidase encoded by the endogenous poxB gene has been reduced or eliminated and any zwf gene is overexpressed.

The Examiner also argues that the specification does not enable the use of microorganisms other than *Corynebacterium glutamicum*, and does not teach: a) how to

amplify genes other than by increasing the copy number or using a strong promoter; b)all methods of modifying the endogenous poxB gene; and c) methods for making amino acids other than L-lysine.

In response, Applicants submit that most of the Examiner's arguments have been overcome by the amendments discussed above. Specifically, claims are now limited to the use of *Corynebacterium glutamicum*, and to forms of zwf and poxB that are defined by the specific sequences they encode.

Applicants respectfully traverse the Examiner's arguments insofar as they allege that claims are not enabled because the specification does not teach all methods for increasing the activity of the zwf gene or decreasing the activity of the poxB gene. Although such allegations would be appropriate if Applicants were claiming methods for modifying the activity of these genes, they are not appropriate for the claims that are presently pending. These claims are directed to methods for producing amino acids using bacteria that have been engineered to have increased zwf gene activity and decreased poxB gene activity. Enablement of this invention only requires that Applicants provide one method by which the invention can be made and used and this has clearly been done in the specification. Any other method for amplifying zwf or decreasing poxB will produce a bacterium that is equally useful in the invention as claimed. It is the bacteria, not the method by which they are made, that is important to the invention.

Applicants also do not agree with the Examiner's allegation that claims should be limited to the production of L-lysine. The ability of bacteria to make each of the amino acids recited in the claims depends upon the availability of metabolic intermediates. This is illustrated in the enclosed diagram (Exhibit A). It can be seen that pyruvate is used in the pathway forming tryptophan and threonine and that threonine is used to form isoleucine. By engineering bacteria in the manner required by the claims, the amount of pyruvate available is increased and, as a result, all of the amino acids whose production depends upon the availability of pyruvate should be formed more efficiently. Because of the central place of pyruvate in the metabolic pathway for the production of amino acids, it is not necessary to

have a separate procedure for the production of lysine, isoleucine, tryptophan, and threonine. It should also be pointed out that Example 2 in which the zwf gene is amplified (albeit, without a corresponding decrease in poxB) demonstrates increased production of *both* lysine and threonine (see, particularly, Example 2.2).

For the reasons provided above, Applicants respectfully submit that the Examiner's rejection of claims based upon the enablement requirement of 35 U.S.C. § 112 has been overcome. It is therefore respectfully requested that this rejection be withdrawn.

Conclusion

In light of the amendments and discussion above, Applicants believe that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims presently pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (202) 419-7013.

Respectfully submitted,

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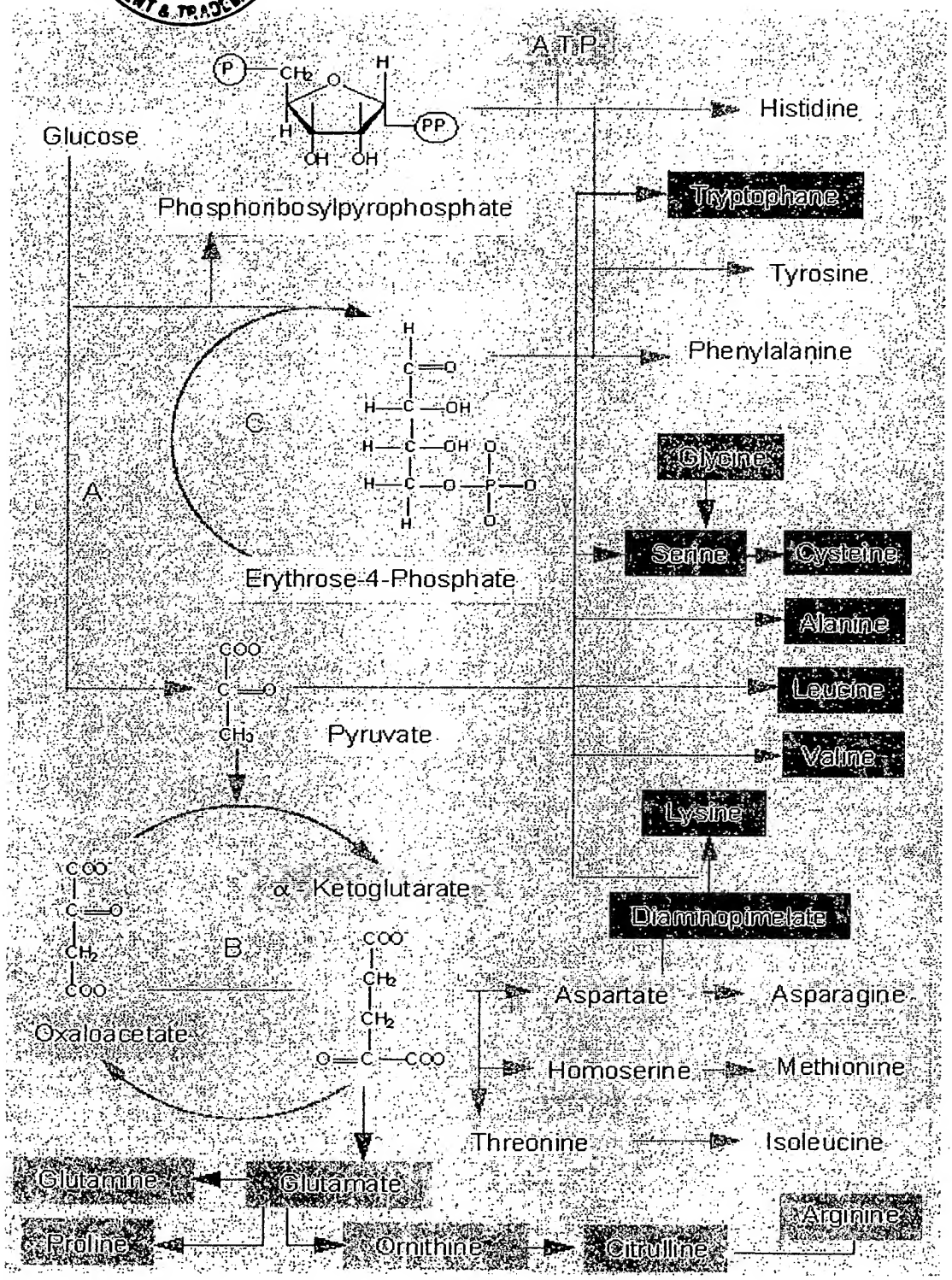

Exhibit A